AMENDMENTS TO THE SPECIFICATION

Please make the following amendments to the specification.

Delete lines 1-341 and 343-10071247 of Table 1.

Delete lines 1-144956 and 145051-12149488 of Table 2A-2C.

Delete lines 1-4458 and 4461-370836 of Table 3.

Delete lines 1-8128 and 8134-675200 of Table 4.

Delete lines 1-5175 and 5178-426687 of Table 5.

Delete lines 1-1178497, 1178499-1355053,1355055-1386259, 1386261-2801043, 2801045-2843615,2843617- 2967385 , 2967387-6221083, 6221085- 6534577, 6534579-6595451, 6595453-8186457, 8186459-9869797, 9869799-12224465, and 12224467-12500005 of Table 6.

Delete lines 1-146393, 146402-146418 and 146423-13520463 of Tables 7A and 7B.

Delete lines 1-435531 and 435560-31620985 of Tables 8A-8F.

Delete lines 1-37972 and 38087-135057 of Table 9.

Delete lines 1-738571 and 738659-1127401 of Table 10.

Delete lines 1-232, 258-327, 372-484, 493-552, 567-754, and 783-873 of Table 12.

Delete lines 1-548 and 550-2537 of Table 13.

Delete lines 1-30, 45-87, 104-122, 135-191, 211-237, 243-341, 352-425, 440-450, 454-546, 550- 607, 609-670, and 689-801 of Table 14.

Delete paragraphs 0026-0235 and replace with the following paragraphs:

> The present invention relates to an isolated nucleic acid of 19 to 24 nucleotides wherein the sequences of the nucleic acid comprise (a) at least 19 consecutive nucleotides of SEQ ID NO: 159, (b) a RNA encoded by (a), (c) a sequence at least 80% identical to (a) or (b); or (d) the complement of any one of (a)-(c), wherein the complement is identical in length to the nucleic acid of (a)-(c). Additionally, the present invention relates to vectors comprising a human insert, wherein the human insert consists of the nucleic acid of 19 to 24 nucleotides wherein the sequences of the nucleic acid comprises (a) at least 19 consecutive nucleotides of SEQ ID NO: 159, (b) a RNA encoded by (a), (c) a sequence at least 80% identical to (a) or (b), or (d) the complement of any one of (a)-(c), wherein the complement is identical in length to the nucleic acid of (a)-(c), and wherein the vector comprises no other human insert but the nucleic acid as described above.

The present invention also relates to an isolated nucleic acid of 50 to 140 nucleotides wherein the sequences of the nucleic acid comprise (a) at least 19 consecutive nucleotides of SEQ ID NO: 159, (b) a RNA encoded by (a), (c) a sequence at least 80% identical to (a) or (b); or (d) the complement of any one of (a)-(c), wherein the complement is identical in length to the nucleic acid of (a)-(c). Additionally, the present invention relates to vectors comprising a human insert, wherein the human insert consists of the nucleic acid of 19 to 24 nucleotides wherein the sequences of the nucleic acid comprises (a) at least 19 consecutive nucleotides of SEQ ID NO: 159, (b) a RNA encoded by (a), (c) a sequence at least 80% identical to (a) or (b), or (d) the complement of any one of (a)-(c), wherein the complement is identical in length to the nucleic acid of (a)-(c), and wherein the vector comprises no other human insert but the nucleic acid as described above.

After the heading, "DETAILED DESCRIPTION" and before paragraph 0276, add the following paragraphs:

The present invention discloses 122,764 novel human regulatory microRNA-like (miRNA) oligonucleotides referred to here as Genomic Address Messenger (GAM) oligonucleotides, which GAM oligonucleotides are detectable using a novel bioinformatic approach, and go undetected by conventional molecular biology methods. Each GAM oligonucleotide specifically inhibits translation of one of more target genes by hybridization of an RNA transcript encoded by the GAM, to a site located in an untranslated region (UTR) of the mRNA of one or more of the target genes. Also disclosed are 18,602 novel microRNA cluster like polynucleotides, referred to here as Genomic Record (GR) polynucleotides.

Accordingly, the invention provides several substantially pure nucleic acids (e.g., genomic DNA, cDNA or synthetic DNA) each comprising a novel human GAM oligonucleotide, vectors comprising the DNAs, probes comprising the DNAs, a method and system for bioinformatic detection of GAM oligonucleotides and their respective targets, laboratory methods for validating expression of GAM oligonucleotides, and a method and system for selectively modulating translation of known target genes of the GAM oligonucleotides.

The present invention represents a scientific breakthrough, disclosing novel miRNA-like oligonucleotides the number of which is dramatically larger than previously believed existed. Prior-art studies reporting miRNA oligonucleotides ((Lau et al., Science 294358-862 (2001), Lagos-Quintana et al., Science 294: 853-858 (2001)) discovered 93 miRNA oligonucleotides in several species, including

21 in human, using conventional molecular biology methods, such as cloning and sequencing.

Molecular biology methodologies employed by these studies are limited in their ability to detect rare miRNA oligonucleotides, since these studies relied on sequencing of a limited number of clones (300 clones by Lau and 100 clones by Lagos-Quintana) of small segments (i.e. size fractionated) of RNA. miRNA oligonucleotides detected in these studies therefore, represent the more prevalent among the miRNA oligonucleotide family, and are typically not be much rarer than 1% of all small -20 nt-long RNA oligonucleotides present in the tissue from the RNA was extracted.

Recent studies state the number of miRNA oligonucleotides to be limited, and describe the limited sensitivity of available methods for detection of miRNA oligonucleotides: "The estimate of 255 human miRNA oligonucleotides is an upper bound implying that no more than 40 miRNA oligonucleotides remain to be identified in mammals" (Lim et al., Science, 299:1540 (2003)); "Estimates place the total number of vertebrate miRNA genes at about 200-250" (Ambros et al. Curr. Biol. 13307-818 (2003)); and "Confirmation of very low abundance miRNAs awaits the application of detection methods more sensitive than Northern blots" (Ambros et al. Curr. Biol. 13.807-818 (2003)).

The oligonucleotides of the present invention represent a revolutionary new dimension of genomics and of biology: a dimension comprising a huge number of non-protein- coding oligonucleotides which modulate expression of thousands of proteins and are associated with numerous major diseases. This new dimension disclosed by the present invention dismantles a central dogma that has dominated life-sciences during the past 50 years, a dogma which has emphasized the importance of protein coding regions of the genome, holding non-protein- coding regions to be of little consequence, often dubbing them "junk DNA".

Indeed, only in November, 2003 has this long held belief as to the low importance of non-protein-coding regions been vocally challenged. As an example, an article titled "The Unseen Genome - Gems in the Junk" (Gibbs, W.W. Sci. Am. 289:46-53 (2003)) asserts that the failure to recognize the importance of non-protein- coding regions "may well go down as one of the biggest mistakes in the history of molecular biology". Gibbs further asserts that "what was damned as junk because it was not understood, may in fact turn out to be the very basis of human complexity. The present invention provides a dramatic leap in understanding specific important roles of non-protein- coding regions. An additional scientific breakthrough of the present invention is a novel conceptual model disclosed by the present invention, which conceptual model is preferably used to encode in a genome the determination of cell differentiation, utilizing

oligonucleotides and polynucleotides of the present invention. Using the bioinformatic engine of the present invention, 122,764 GAM oligonucleotides and their respective precursors and targets have been detected. These bioinformatic predictions are supported by robust biological studies. Microarray experiments validated expression of 2,534 GAM oligonucleotides out of a sample of 8,244 tested. Of these, 1,114 GAM oligonucleotides scored extremely highly: over six standard deviations higher than the background noise of the microarray, and over two standard deviations above their individual mismatch control probes. Thirty eight GAM oligonucleotides were sequenced.

In various preferred embodiments, the present invention seeks to provide an improved method and system for specific modulation of the expression of specific target genes involved in significant human diseases. It also provides an improved method and system for detection of the expression of novel oligonucleotides of the present invention, which modulate these target genes. In many cases, the target genes may be known and fully characterized, however in alternative embodiments of the present invention, unknown or less well characterized genes may be targeted.

A "Nucleic acid" is defined as a ribonucleic acid (RNA) molecule, or a deoxyribonucleic acid (DNA) molecule, or complementary deoxyribonucleic acid (cDNA), comprising either naturally occurring nucleotides or non-naturally occurring nucleotides. "Substantially pure nucleic acid", "Isolated Nucleic Acid", "Isolated Oligonucleotide" and "Isolated Polynucleotide" are defined as a nucleic acid that is free of the genome of the organism from which the nucleic acid is derived, and include, for example, a recombinant nucleic acid which is incorporated into a vector, into an autonomously replicating plasmid or virus, or into the genomic nucleic acid of a prokaryote or eukaryote at a site other than its natural site; or which exists as a separate molecule (e.g., a cDNA or a genomic or cDNA fragment produced by PCR or restriction endonuclease digestion) independent of other nucleic acids.

An "Oligonucleotide" is defined as a nucleic acid comprising 2-139 nts, or preferably 16-120 nts. A "Polynucleotide" is defined as a nucleic acid comprising 140-5000 nts, or preferably 140-1000 nts.

A "Complementary" sequence is defined as a first nucleotide sequence which reverses complementary of a second nucleotide sequence: the first nucleotide sequence is reversed relative to a second nucleotide sequence, and wherein each nucleotide in the first nucleotide sequence is complementary to a corresponding nucleotide in the second nucleotide sequence (e.g. ATGGC is the complementary sequence of GCCAT).

"Hybridization", "Binding" and "Annealing" are defined as hybridization, under in-vivo physiological conditions, of a first nucleic acid to a second nucleic acid, which second nucleic acid is at least partially complementary to the first nucleic acid.

A "Hairpin Structure" is defined as an oligonucleotide having a nucleotide sequence that is 50-140 nts in length, the first half of which nucleotide sequence is at least partially complementary to the second part thereof, thereby causing the nucleic acid to fold onto itself, forming a secondary hairpin structure.

A "Hairpin-Shaped Precursor" is defined as a Hairpin Structure which is processed by a Dicer enzyme complex, yielding an oligonucleotide which is about 19 to about 24 nts in length. "Inhibiting translation" is defined as the ability to prevent synthesis of a specific protein encoded by a respective gene by means of inhibiting the translation of the mRNA of this gene. For example, inhibiting translation may include the following steps: (1) a DNA segment encodes an RNA, the first half of whose sequence is partially complementary to the second half thereof; (2) the precursor folds onto itself forming a hairpin-shaped precursor; (3) a Dicer enzyme complex cuts the hairpin-shaped precursor yielding an oligonucleotide that is approximately 22 nt in length; (4) the oligonucleotide binds complementarily to at least one binding site, having a nucleotide sequence that is at least partially complementary to the oligonucleotide, which binding site is located in the mRNA of a target gene, preferably in the untranslated region (UTR) of a target gene, such that the binding inhibits translation of the target protein. A "Translation inhibitor site" is defined as the minimal nucleotide sequence sufficient to inhibit translation.

The present invention describes novel miRNA oligonucleotides, detected using a bioinformatic engine described hereinabove. The ability of this detection engine has been demonstrated using stringent algorithmic criteria, showing that the engine has both high sensitivity, indicated by the high detection rate of published miRNAs and their targets, as well as high specificity, indicated by the low amount of "background" hairpin candidates passing its filters. Laboratory tests, based both on sequencing of predicted miRNA oligonucleotides and on microarray experiments, validated 2534 of the miRNA oligonucleotides in the present invention. Further, at least one of these validated miRNA oligonucleotides binds to 1953 of the 203 1 target genes described in the present invention.

There is thus provided in accordance with a preferred embodiment of the present invention a bioinformatically detectable isolated oligonucleotide which is endogenously processed from a hairpin-shaped precursor, and anneals to a portion of a mRNA transcript of a target gene, wherein binding of the oligonucleotide to the mRNA transcript represses expression of the target gene, and wherein the

oligonucleotide has at least 80% sequence identity with a nucleotide sequence selected from the group consisting of SEQ ID NOS: 1-380 and 6894883 - 7033873.

Delete paragraph 0319 and replace it with the following paragraphs:

The nucleotide sequences of each of a plurality of GAM oligonucleotides described by Fig.8. Specifically, in Table 1, line 342 describes GAM RNA (miRNA) as set forth in SEQ ID NO: 159 is shown as predicted from human.

GAM SEQ-ID	GAM NAME	GAM RNA SEQUENCE	GAM ORGANISM	GAM POS
159	GAM345990	ACAAAGCGCTTCTCTTTAGAGT	Homo sapiens	A

In Table 2, lines 144957 - 145050, describes GAM PRECURSOR RNA (hairpin) as set forth in SEQ ID NO: 6821380 and as it relates to Figures 1-8 .

GAM NAME	GAM ORGANISM	PRECUR SEQ-ID	PRECURSOR SEQUENCE	GAM DESCRIPTION
GAM 345990	Human	682138 0	TCTCATGCTG TGACTCTCTG GAGGGAAGCA CTTTCTGTTG TCTGAAAGAA AACAAAGCGC TTCTCTTTAG AGTGTTACGG TTTGAGA	Fig. 8 further provides a conceptual description of another novel bioinformatically-detected human nucleotide of the present invention referred to here as the Genomic Address Messenger 345990 (GAM345990) whose function and utility are known in the art. GAM345990 is a novel bioinformatically Detectable regulatory non-protein-coding, miRNA-like oligonucleotide. The method by which GAM345990 is detected is described with additional reference to Figs. 8-15. The GAM345990 precursor, herein designated GAM PRECURSOR, is encoded by the Human genome .GAM345990 target gene, herein designated GAM TARGET GENE, is a target gene encoded by the human genome The GAM345990 precursor, herein designated GAM PRECURSOR, encodes a GAM345990 precursor RNA, herein designated GAM PRECURSOR RNA. Similar to other miRNA oligonucleotides, the GAM345990 precursor RNA does not encode a protein. GAM345990 precursor RNA folds onto itself, forming GAM345990 folded precursor RNA, herein designated GAM FOLDED PRECURSOR RNA, which has a two-dimensional "hairpin" structure. GAM PRECURSOR RNA folds onto itself forming GAM FOLDED PRECURSOR RNA, which has a two-dimensional "hairpin structure". As is well-known in the art, this "hairpin structure" is typical of RNA encoded by known miRNA-precursor oligonucleotides and is due to the full or partial complementarity of the

nucleotide sequence of the first half of an miRNA -precursor to theRNA that is encoded by a miRNA oligonucleotide to the nucleotide sequence of the second half thereof. A nucleotide sequence that is identical or highly similar to the nucleotide sequence of the GAM345990 precursor RNA is designated SEQ ID NO:6821380, and is provided hereinbelow with reference to the sequence listing section. The nucleotide sequence designated SEQ ID NO:6821380 is located from position 58903810 to position 58903896 relative to chromosome 19 on the "+" strand, and overlaps an intergenic region (UCSC.h16.refGene database).. A schematic representation of a predicted secondary folding of GAM345990 folded precursor RNA, herein designated GAM FOLDED PRECURSOR RNA is set forth in Table 4 incorporated herein. An enzyme complex designated DICER COMPLEX, an enzyme complex composed of Dicer RNaseIII together with other necessary proteins, cuts the GAM345990 folded precursor RNA yielding a single-stranded ~22 nucleotide-long RNA segment designated GAM345990 RNA, herein designated GAM RNA,.Table 5 provides a nucleotide sequence that is highly likely to be identical or extremely similar to the nucleotide sequence of GAM345990 RNA, hereby incorporated herein.

GAM345990 target gene, herein designated GAM TARGET GENE, encodes a corresponding messenger RNA, designated GAM345990 target RNA, herein designated GAM TARGET RNA. As is typical of mRNA of a protein-coding gene, GAM345990 target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein-coding region and 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR, respectively. GAM345990 RNA, herein designated GAM RNA, binds complementarily to one or more target binding sites located in the untranslated regions of GAM345990 target RNA. This complementary binding is due to the partial or full complementarity between the nucleotide sequence of GAM345990 RNA and the nucleotide sequence of each of the target binding sites. As an illustration, Fig. 8 shows three such target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III, respectively. It is appreciated that the number of target binding sites shown in Fig. 8 is only illustrative and that any suitable number of target binding sites may be present. It is further appreciated that although Fig. 8 shows target binding sites only in the 3'UTR region, these target binding sites may instead be located in the 5'UTR region or in both the 3'UTR and 5'UTR regions. The complementary binding of GAM345990 RNA, herein designated GAM RNA, to target binding sites on GAM345990 target RNA, herein designated GAM TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits the translation of GAM345990 target RNA into repsective GAM345990 target protein, herein designated GAM TARGET PROTEIN, shown surrounded by a broken line.

It is appreciated that the GAM345990 target gene,

herein designated GAM TARGET GENE, in fact represents a plurality of GAM345990 target genes. The mRNA of each one of this plurality of GAM345990 target genes comprises one or more target binding sites, each having a nucleotide sequence which is at least partly complementary to GAM345990 RNA, herein designated GAM RNA, and which when bound by GAM345990 RNA causes inhibition of translation of the GAM345990 target mRNA into a corresponding GAM345990 target protein The mechanism of the translational inhibition that is exerted by GAM345990 RNA, herein designated GAM RNA, on one or more GAM345990 target genes, herein collectively designated GAM TARGET GENE, may be similar or identical to the known mechanism of translational inhibition exerted by known miRNA oligonucleotides. The nucleotide sequence of GAM345990 precursor RNA, herein designated GAM PRECURSOR RNA, its respective genomic source and genomic location and a schematic representation of a predicted secondary folding of GAM345990 folded precursor RNA, herein designated GAM FOLDED PRECURSOR RNA are set forth in Tables 3-4, hereby incorporated herein. The nucleotide sequences of a "diced" GAM345990 RNA, herein designated GAM RNA, from GAM345990 folded precursor RNA are set forth in Table 5, hereby incorporated herein. The nucleotide sequences of target binding sites, such as BINDING SITE I, BINDING SITE II and BINDING SITE III of Fig. 8, found on GAM345990 target RNA, herein designated GAM TARGET RNA, and a schematic representation of the complementarity of each of these target binding sites to GAM345990 RNA, herein designated GAM RNA, are set forth in Tables 6-7, hereby incorporated herein. It is appreciated that the specific functions and accordingly the utilities of GAM345990 RNA are correlated with and may be deduced from the identity of the GAM345990 target gene inhibited thereby, and whose functions are set forth in Table 8, hereby incorporated herein.

Table 3 , lines 4,459-4460, shows data relating to the source and location of the GAM oligonucleotide, specificaly the GAM PRECRSOR (hairpin) and its position in the genomic sequence of human.

GAM NAME	PRECUR GAM SEQ-ID	ORGANISM	SOURCE STR AND	SRC-START OFFSET	SRC-END OFFSET
GAM345990	682138 0	Human	19 +	58903810	58903896

Delete paragraph 0320 and replace it with the following paragraphs:

The nucleotide sequences of GAM PRECURSOR RNAs, and a schematic representation of a predicted secondary folding of GAM FOLDED PRECURSOR RNAs, of each of a plurality of GAM oligonucleotides described by Fig. 8 are set forth in Table 4 ,hereby incorporated herein. Table 4 lines 8129-8133, shows a schematic representation of the GAM folder precursor as set forth in SEQ ID NO:159 , beginning at the 5' end (beginning of upper row) to the 3' end (beginning of lower row), where the hairpin loop is positioned at the right part of the drawing .

GAM NAME	PRECUR SEQ-ID	GAM ORG ANISM	PRECURSOR-SEQUENCE	GAM FOLDED PRECURSOR RNA
GAM 345 990	682138 0	Human	TCTCATGCTGTGACTCTCTG GAGGGAAGCACTTTCTGTTG TCTCA GCTGTGAC CTCTGGAGGGAAGC CTT TGTT TC TCTGAAAGAAAACAAAGCGC AGAGT TGGCATTG GAGATTTCTCTTCG GAA ACAA AG TTCTCTTTAGAGTGTTACGG TTTGAGA	T T A TC G TG \ A T T C -- A AA

Delete paragraph 0321 and replace it with the following paragraphs:

The nucleotide sequences of diced` GAM RNAs of each of a plurality of GAM oligonucleotides described by Fig. 8 are set forth in **Table 5**, hereby incorporated herein.Table 5 , line 5176- 5177 shows the mature GAM RNA as set forth in SEQ ID NO: 682138 as sliced by DICER from the GAM PRECURSOR sequence (hairpin) as set forth in SEQ ID NO: 682138.

GAM NAME	GAM ORGANISM	GAM RNA SEQUENCE	PRECUR SEQ-ID	GAM POS
GAM345990	Human	ACAAAGCGCTTCTCTTTAGAGT	682138	A

Delete paragraph 0322 and replace it with the following paragraphs:

The Nucleotide sequences of target binding sites, such as BINDING SITE I, BINDING SITE II and BINDING SITE III found on GAM TARGET RNAs of each of a plurality of GAM oligonucleotides described by Fig. 1, and a schematic representation of the complementarity of each of these target binding sites to each of a plurality of GAM RNAs described by Fig. 8 are set forth in Tables 6-7, hereby incorporated herein. Table 6 shows data relating to the SEQ ID NO of the GAM target binding

site sequence of the target gene name as bound by the GAM RNA as set forth in SEQ ID NO: 159. Table 6, lines1355054, 2843616, 6221084, 8186458, 9869798, 1222446, 1386260, 2801044, 6534578, 1178498, 2967386, 6595452 related to target binding site SEQ ID NO: 783894, 1517754, 3173983, 4136777, 4962915, 6130451, 799345, 1496799, 3328443, 696840, 1578845 , and 3358376 respectively.

TARGET BINDING SITE SEQ-ID	TARGET ORGANISM	TARGET	TARGET BINDING SITE SEQUENCE
783894	Homo sapiens	EGFR	CTAAGGATAGCACCGCTTTT
1517754	Homo sapiens	EGFR	CTAAGGATAGCACCGCTTTT
3173983	Homo sapiens	EGFR	CTAAGGATAGCACCGCTTTT
4136777	Homo sapiens	EGFR	CTAAGGATAGCACCGCTTTT
4962915	Homo sapiens	EGFR	CTAAGGATAGCACCGCTTTT
6130451	Homo sapiens	EGFR	CTAAGGATAGCACCGCTTTT
799345	Homo sapiens	EGFR	TTAACAGCAGTCCTTTGT
1496799	Homo sapiens	EGFR	TTAACAGCAGTCCTTTGT
3328443	Homo sapiens	EGFR	TTAACAGCAGTCCTTTGT
696840	Homo sapiens	EGFR	CAAACCCCCTCCTTACGCTTTGT
1578845	Homo sapiens	EGFR	CAAACCCCCTCCTTACGCTTTGT
3358376	Homo sapiens	EGFR	CAAACCCCCTCCTTACGCTTTGT

Table 7, lines 146,394-146,401 and 146,419-146,422 shows data relating to target genes and binding site of GAM oligonucleotides.

GAM NAME	GAM ORG ANISM	GAM RNA SEQUENCE	TARGET BS-SEQ	TARGET REF-ID	TARGET ORGANISM	TARGET (UPPER:GAM;LOWER:TARGET)	UTR BINDING-SITE DRAW
GAM 345 990	Human	ACAAAGCG CTTCTCTT TAGAGT	CAAACCCC EGFR CTCCTTAC GCTTTGT	NM_ 005228	Human	3 CCCCCTCCTTA C AAA CGCTTTGT G TTT GCGAAACA TGA A CTCTTC-----	A
GAM 345 990	Human	ACAAAGCG CTTCTCTT TAGAGT	CTAAGGAT EGFR AGCACCGC TTTT	NM_ 005228	Human	3 - T CAC - CTAAGGA AG CGCTTT T GATTTCT TT GCGAAA A	A
GAM 345 990	Human	ACAAAGCG CTTCTCTT TAGAGT	TTAACAGC EGFR AGTCCTTT GT	NM_ 005228	Human	3 C CA T- - T TAA AG G C CTTTGT A ATT TC T G GAAACA TG G - TC TC C	A

Delete paragraph 0323 and replace it with the following paragraphs:

It is appreciated that specific functions and accordingly utilities of each of a plurality of GAM oligonucleotides described by Fig.8 are correlated with, and may be deduced from the identity of the GAM TARGET GENEs inhibited thereby, and whose functions are set forth in Table 8, hereby incorporated herein. Table 8 , lines 435532-435559 shows data relating to the function and utilities of GAM RNA as set forth in SEQ ID NO: 159.

GAM NAME	GAM RNA SEQUENCE	GAM ORGANISM	TARGET	TARGET	GAM FUNCTION	GAM POS
GAM 3459 90	ACAAAGCG CTTCTCTT TAGAGT	Human	EGFR	Human	Epidermal growth factor receptor (EGFR, Accession number : A NM_005228) is another GAM345990 target gene that is encoded by the human genome. EGFR BINDING SITE 1 through EGFR BINDING SITE 3 are human target binding sites that are found in the untranslated regions of mRNA encoded by the EGFR gene,corresponding to target binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 8. Additionally, using the Binding site prediction system of the present invention GAM345990-A binds to sequences on orthologous UTR of(NM_031507). The nucleotide sequences of EGFR BINDING SITE 1 through EGFR BINDING SITE 3, and the complementarity secondary structure to the nucleotide sequence of GAM345990 RNA are set forth in Tables 6-7, hereby incorporated herein. Another function of GAM345990 is to inhibit EGFR, a GAM345990 human target gene which is involved in the control of cell growth and differentiation. EGFR is associated with Nonsmall cell lung cancer, Small cell carcinoma, Lung cancer, Breast cancer and Colorectal cancer diseases, and therefore GAM345990 is associated with the abovementioned diseases. Accordingly, the utilities of GAM345990 include the diagnosis, prevention and treatment of Nonsmall cell lung cancer, Small cell carcinoma, Lung cancer, Breast cancer and Colorectal cancer and of other diseases and clinical conditions associated with EGFR. The function of EGFR and its association with various diseases and clinical conditions has been established by previous studies, as described hereinabove with reference to GAM338539.	

Delete paragraph 0324 and replace it with the following paragraphs:

Studies documenting the well known correlations between each of a plurality of GAM TARGET GENEs that are described by Fig. 8 and the known gene functions and related diseases are listed in Table 9 lines 37973-38086 hereby incorporated herein.

TARGET	TARGET ORGANISM	REFERENCES
EGFR	Human	Aden, D. P.; Knowles, B. B.: Cell surface antigens coded for by the human chromosome 7. Immunogenetics 3: 209-211, 1976.
EGFR	Human	Carlin, C. R.; Aden, D. P.; Knowles, B. B.: S6 is the human receptor for epidermal growth factor (EGF). (Abstract) Cytogenet. Cell Genet. 32: 256 only,1982.
EGFR	Human	Carlin, C. R.; Knowles, B. B.: Identity of human epidermal growth factor (EGF) receptor with glycoprotein SA-7: evidence for differential phosphorylation of the two components of the EGF receptor from A431 cells. Proc. Nat. Acad. Sci.79: 5026-5030, 1982.
EGFR	Human	Carpenter, G.: Properties of the receptor for epidermal growth factor. Cell 37:357-358, 1984.
EGFR	Human	Chen, B.; Bronson, R. T.; Klaman, L. D.; Hampton, T. G.; Wang, J.; Green, P. J.;Magnuson, T.; Douglas, P. S.; Morgan, J. P.; Neel, B. G.: Mice mutant for Egfr and Shp2 have defective cardiac semilunar valvulogenesis. Nature Genet. 24:296-299, 2000.
EGFR	Human	Davies, R. L.; Grosse, V. A.; Kucherlapati, R.; Bothwell, M.: Genetic analysis of epidermal growth factor action: assignment of human epidermal growth factor receptor gene to chromosome 7. Proc. Nat. Acad. Sci. 77: 4188-4192, 1980.
EGFR	Human	Downward, J.; Yarden, Y.; Mayes, E.; Scrace, G.; Totty, N.; Stockwell, P.; Ullrich, A.; Schlessinger, J.; Waterfield, M. D.: Close similarity of epidermal growth factor receptor and v-erb-B oncogene protein sequences. Nature 307:521-527, 1984.
EGFR	Human	Haley, J.; Whittle, N.; Bennett, P.; Kinchington, D.; Ullrich, A.; Waterfield,M.: The human EGF receptor gene: structure of the 110 kb locus and identification of sequences regulating its transcription. Oncogene Res. 1:375-396, 1987.
EGFR	Human	Henn, W.; Blin, N.; Zang, K. D.: Polysomy of chromosome 7 is correlated with overexpression of the erbB oncogene in human glioblastoma cell lines. Hum.Genet. 74: 104-106, 1986.
EGFR	Human	Kondo, I.; Shimizu, N.: Mapping of the human gene for epidermal growth factor receptor (EGFR) on the p13-q22 region of chromosome 7. Cytogenet. Cell Genet.35: 9-14, 1983.
EGFR	Human	Kramer, A.; Yang, F.-C.; Snodgrass, P.; Li, X.; Scammell, T. E.; Davis, F. C.;Weitz, C. J.: Regulation of daily locomotor activity and sleep by hypothalamic EGF receptor signaling. Science 294:

2511-2515, 2001.

EGFR Human Lanzetti, L.; Rybin, V.; Malabarba, M. G.; Christoforidis, S.; Scita, G.; Zerial, M.; Di Fiore, P. P.: The Eps8 protein coordinates EGF receptor signalling through Rac and trafficking through Rab5. Nature 408: 374-377, 2000.

EGFR Human Maciag, T.: The human epidermal growth factor receptor-kinase complex. Trends Biochem. Sci. 7: 1-2, 1982.

EGFR Human Pai, R.; Soreghan, B.; Szabo, I. L.; Pavelka, M.; Baatar, D.; Tarnawski, A. S.: Prostaglandin E2 transactivates EGF receptor: a novel mechanism for promoting colon cancer growth and gastrointestinal hypertrophy. Nature Med. 8: 289-293,2002.

EGFR Human Privalsky, M. L.; Ralston, R.; Bishop, J. M.: The membrane glycoprotein encoded by the retroviral oncogene v-erb-B is structurally related to tyrosine-specific protein kinases. Proc. Nat. Acad. Sci. 81: 704-707, 1984.

EGFR Human Reynolds, F. H., Jr.; Todaro, G. J.; Fryling, C.; Stephenson, J. R.: Human transforming growth factors induce tyrosine phosphorylation of EGF receptors. Nature 292: 259-262, 1981.

EGFR Human Shimizu, N.; Behzadian, M. A.; Shimizu, Y.: Genetics of cell surface receptors for bioactive polypeptides: binding of epidermal growth factor is associated with the presence of human chromosome 7 in human-mouse cell hybrids. Proc. Nat. Acad. Sci. 77: 3600-3604, 1980.

EGFR Human Sibilia, M.; Fleischmann, A.; Behrens, A.; Stingl, L.; Carroll, J.; Watt, F. M.; Schlessinger, J.; Wagner, E. F.: The EGF receptor provides an essential survival signal for SOS-dependent skin tumor development. Cell 102: 211-220, 2000.

EGFR Human Silver, J.; Whitney, J. B., III; Kozak, C.; Hollis, G.; Kirsch, I.: Erbb is linked to the alpha-globin locus on mouse chromosome 11. Molec. Cell. Biol. 5: 1784-1786, 1985.

EGFR Human Spurr, N. K.; Goodfellow, P. N.; Solomon, E.; Parkar, M.; Vennstrom, B.; Bodmer, W. F.: Mapping of cellular oncogenes; erb B on chromosome 7. (Abstract) Cytogenet. Cell Genet. 37: 590 only, 1984.

EGFR Human Spurr, N. K.; Solomon, E.; Jansson, M.; Sheer, D.; Goodfellow, P. N.; Bodmer, W. F.; Vennstrom, B.: Chromosomal localisation of the human homologues to the oncogenes erbA and B. EMBO J. 3: 159-163, 1984.

EGFR Human Thaung, C.; West, K.; Clark, B. J.; McKie, L.; Morgan, J. E.; Arnold, K.; Nolan, P. M.; Peters, J.; Hunter, A. J.; Brown, S. D. M.; Jackson, I. J.; Cross, S. H.: Novel ENU-induced eye mutations in the mouse: models for human eye disease. Hum. Molec. Genet. 11: 755-767, 2002.

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Delete paragraph 0378 and replace it with the following paragraphs:

In order to validate the efficacy and accuracy of the Dicer-cut location detector 116, a sample of novel oligonucleotides detected thereby is preferably selected, and validated by wet lab experiments. Laboratory results validating the efficacy of the Dicer-cut location detector 116 are described hereinbelow with reference to Figs. 22-24D, Fig 27 and also in the enclosed file TABLE_13 line 549.

GAM RNA SEQUENCE	VALIDATION METHOD	SIGNAL Z-SCORE	BACKGROUND Z-SCORE	MISMATCH Z-SCORE	GAM RNA SEQ-ID
ACAAAGCGCTTCTCTTTAGAGT	Chip strong	65518	11.238881	26.766436	159

Delete paragraph 0596 and replace it with the following paragraphs:

Table 10 lines 738572-738658 comprises data relating to novel GR polynucleotides of the present invention, and contains the following fields: GR NAME: Rosetta Genomics Ltd.nomenclature (see below);

GR ORGANISM: identity of the organism encoding the GR polynucleotide; GR DESCRIPTION: Detailed description of a GR polynucleotide, with reference to Fig. 16;

GR NAME	GR ORGANISM	GR DESCRIPTION
GR12177	Human	Fig. 16 further provides a conceptual description of another bioinformatically-detected regulatory human polynucleotide referred to in this Table as the Genomic Record 12177 (GR12177) polynucleotide. GR12177 encodes an operon-like cluster of novel miRNA-like oligonucleotides, each of which in turn modulates the expression of at least one target gene. The function and utility of at least one target gene is known in the art. The GR12177 precursor, herein designated GR PRECURSOR, is a novel, bioinformatically-detected, regulatory, non-protein-coding polynucleotide. The method by which the GR12177 precursor is detected is described hereinabove with additional reference to Figs. 9-18. The GR12177 precursor encodes GR12177 precursor RNA, herein designated GR PRECURSOR RNA that is typically several hundred to several thousand nucleotides long. The nucleotide sequence of human GR12177 is located from position 58908413 to 58908500 on the "+" strand of chromosome 19. The GR12177 precursor RNA folds spatially, forming the GR12177 folded precursor RNA, herein designated GR FOLDED PRECURSOR RNA. It is appreciated that the GR12177 folded precursor RNA comprises a plurality of what is known in the art as hairpin structures. Hairpin structures result from the presence of segments of the nucleotide sequence of GR12177 precursor RNA in which the first half of each such segment has a nucleotide sequence which is at least a partial, and sometimes an accurate, reverse-complement sequence of the second half thereof, as is well known in the art. The GR12177 folded precursor RNA, herein designated GR FOLDED PRECURSOR RNA is naturally processed by cellular enzymatic activity into at least 5 separate GAM precursor RNAs GAM355613 precursor RNA, GAM355614 precursor RNA, GAM345990 precursor RNA, GAM355615 precursor RNA and GAM355616 precursor RNA, herein Schematically represented by GAM1 FOLDED PRECURSOR RNA through GAM3 FOLDED PRECURSOR RNA. Each GAM folded precursor RNA is a hairpin-shaped RNA segment, corresponding to GAM FOLDED PRECURSOR RNA of Fig. 8. The abovementioned GAM folded precursor RNAs are diced by DICER COMPLEX of Fig. 8, yielding short RNA segments of about 22 nucleotides in length GAM355613 RNA GAM355614 RNA, GAM345990 RNA, GAM355615 RNA and GAM355616 RNA, repectively, herein schematically represented by GAM1 RNA through GAM3 RNA. Each human GAM RNA corresponds to GAM RNA of Fig. 8. GAM355613 RNA, herein schematically represented by GAM1 RNA through GAM3 RNA binds complementarily to a target binding site located in an untranslated region of GAM355613 target RNA, herein schematically represented by GAM1 TARGET RNA through GAM3 TARGET RNA. The target binding site corresponds to BINDING SITE I, BINDING SITE II and BINDING SITE III of Fig. 8. The binding of the GAM RNA to its target RNA inhibits the translation of GAM355613 target RNA into GAM355613 target protein herein schematically represented by GAM1 TARGET PROTEIN through GAM3 TARGET PROTEIN, all corresponding to GAM TARGET PROTEIN of Fig. 8. GAM355614 RNA, herein schematically represented by GAM1 RNA through GAM3 RNA, binds complementarily to a target binding site located in an untranslated region of GAM355614 target RNA, herein schematically represented by GAM1 TARGET RNA through GAM3 TARGET RNA. The target binding site corresponds to BINDING SITE I, BINDING SITE II and BINDING SITE III of Fig. 8. The binding of the

GAM RNA to its target RNA inhibits the translation of GAM355614 target RNA into GAM355614 target protein herein schematically represented by GAM1 TARGET PROTEIN through GAM3 TARGET PROTEIN all corresponding to GAM TARGET PROTEIN of Fig. 8. GAM345990 RNA, herein schematically represented by GAM1 RNA through GAM3 RNA, binds complementarily to a target binding site located in an untranslated region of GAM345990 target RNA, herein schematically represented by GAM1 TARGET RNA through GAM3 TARGET RNA. The target binding site corresponds to BINDING SITE I, BINDING SITE II and BINDING SITE III of Fig. 8. The binding of the GAM RNA to its target RNA inhibits the translation of GAM345990 target RNA into GAM345990 target protein, herein schematically represented by GAM1 TARGET PROTEIN through GAM3 TARGET PROTEIN, all corresponding to GAM TARGET PROTEIN of Fig. 8. GAM355615 RNA, herein schematically represented by GAM1 RNA through GAM3 RNA, binds complementarily to a target binding site located in an untranslated region of GAM355615 target RNA, herein schematically represented by GAM1 TARGET RNA through GAM3 TARGET RNA. The target binding site corresponds to BINDING SITE I, BINDING SITE II and BINDING SITE III of Fig. 8. The binding of the GAM RNA to its target RNA inhibits the translation of GAM355615 target RNA into GAM355615 target protein, herein schematically represented by GAM1 TARGET PROTEIN through GAM3 TARGET PROTEIN, all corresponding to GAM TARGET PROTEIN of Fig. 8. GAM355616 RNA, herein schematically represented by GAM1 RNA through GAM3 RNA, binds complementarily to a target binding site located in an untranslated region of GAM355616 target RNA, herein schematically represented by GAM1 TARGET RNA through GAM3 TARGET RNA. The target binding site corresponds to BINDING SITE I, BINDING SITE II and BINDING SITE III of Fig. 8. The binding of the GAM RNA to its target RNA inhibits the translation of GAM355616 target RNA into GAM355616 target protein, herein schematically represented by GAM1 TARGET PROTEIN through GAM3 TARGET PROTEIN, all corresponding to GAM TARGET PROTEIN of Fig. 8. It is appreciated that the specific functions, and accordingly the utilities, of the GR12177 polynucleotide are correlated with and may be deduced from the identity of the target genes that are inhibited by GAM RNAs that are present in the operon-like cluster of the polynucleotide. Thus, for the GR12177 polynucleotide, it is the GAM355613 target protein, GAM355614 target protein, GAM345990 target protein, GAM355615 target protein and GAM355616 target protein, herein schematically represented by GAM1 TARGET PROTEIN through GAM3 TARGET PROTEIN that are inhibited by the GAM RNA. The function of the GAM355613, GAM355614, GAM345990, GAM355615 and GAM355616 target genes is elaborated in Table 8.

Delete paragraph 0598 and replace it with the following paragraph:

Table 12 lines 233-257, 328- 371, 485-492, 553-566, 755-782 comprises data relating to diseases that GAM oligonucleotides are predicted to regulate the disease- associated genes. Each row is referred to a specific disease, and lists the GAM target genes related to the disease. The first row is a summary of ALL diseases containing in the present invention, thus listing ALL GAM target genes relating to theses diseases. The table contains the following fields: ROW#: index of the row number; DISEASE NAME: name of the disease; TARGET-GENES ASSOCIATED WITH DISEASE: list of GAM target genes that are associated with the specified disease;

This is the OMIM table, describing the relation between genes and diseases.

ROW#	DISEASE NAME	TARGET-GENES ASSOCIATED WITH DISEASE
16	lung cancer	ABCC1, ABCC3, ABCC4, ABCC5, ABCG2, ACE, ADCYAP1, ADPRT, AHR, AKT1, AKT2, AKT3, ALDOA, ALOX5, ANXA2, AR, ARHA, AVP, AXL, BAI1, BAK1, BAX, BCHE, BCL10, BCL2, BCL2L1, BGLAP, BIRC5, BRAF, BRS3, BUB1, CALCA, CASP3, CASP8, CASP9, CAT, CAV1,CCKBR, CCL2, CCL4, CCND1, CD151, CD24, CD44, CD59, CD74, CDC2, CDH13, CDK2, CDK4, CDKN1A, CDKN1B, CDKN2B, CDKN2D, CEACAM1, CEACAM5, CEBPA, CGA, CHGA, CHGB, CNK, CP, CR1, CREB1, CRH, CRMP1, CSF3, CST3, CTAG1, CTSB, CTSH, CTSS, CXCL10, CXCL5, CYP1A1, CYP1B1, CYP2D6, DAF, DAPK1, DES, DLEC1, DNMT3B, DPYSL5, DRD2, DTR, EFNA1, EGFR, EGR1, EIF2S1, EIF4E, ELF3, ENG, ENO1, ENO2, ENO3, EPHA2, EPO, ERBB2, ERCC5, ETV4, FASN, FES, FIGF, FLJ22795, FLT1, FLT4, FOS, FOSL1, FURIN, FUT4, FUT7, GADD45A, GADD45B, GADD45G, GHRHR, GNAI2, GPX1, GRPR, GSN, GSTM1, GSTM3, GSTP1, HMGA1, HMGA2, HMGCR, HNRPA2B1, HOXA1, HOXA7, HOXD3, HSPG2, HYAL2, IFNG, IGF1R, IGF2, IGF2R, IGFBP2, IGFBP4, IGSF4, IL10, IL15, IL1A, IL1B, IL1RN, IL24, IL2RB, IL6ST, IRF1, ITGA2, ITGA6, ITGA9, JUN, KAI1, KIT, KITLG, KRT14, KRT18, KRT7, LAMR1, LCK, LCN1, LDLR, LGALS1, LMNA, LMO2, LOST1, LPP, LTA, MAD, MADH4, MALT1, MAPK1, MAPKAPK3, MCC, MDK, MDM2, MEN1, MEST, MHC2TA, MME, MMP1, MMP2, MMP9, MPO, MSLN, MST1, MST1R, MTAP, MTHFR, MUC1, MUC4, MYCL1, MYCN, MYO18B, NCAM1, NF1, NME1, NOS3, NQO1, NR3C1, NR4A1, OGG1, ORM1, ORM2, OXT, PACE4, PAM, PAX7, PBOV1, PCSK1, PECAM1, PGF, PGGT1B, PIGR, PKM2, PLAT, PLAU, PLCL1, PLK, POMC, POR, PPP2R1B, PRDM2, PRKCM, PTMA, PTPRG, PTPRJ, RAD51L1 , RASA1, RASSF1, RB1, RBL2, RBM6, RBP1L1, RCV1, RELA, RNF7, RPA1, RPS6, RPS6KA1, RTN1, SDC1, SELE, SEMA3B, SEMA3F, SERPINE1, SFTPA1, SFTPB, SFTPC, SHH, SKP2, SLC22A1L, SLC2A1, SLC2A2, SLC2A3, SLPI, SP1, SPINT2, SPN, SSX2, TAC1, TBXA2R, TEK, TERT, TF, TFRC, TGFB3, TGFBR2, TGM2, THBD, THPO, TIMP2, TITF1, TNC, TNF, TNFRSF10C, TNFRSF1B, TNFRSF5, TNFRSF9, TNFSF10, TNFSF6, TOP2B, TP53, TP73, TP73L, TPM2, TPX2, TSC1, USP4, VIP, WNT7A AND WT1.
37	Breast cancer	ABCC1, ABCG2, ABL1, ACE, ACP5, ACTB, ACTN4, ACVR1, ADAM11, ADPRT, AHR, AKT1, AKT2, AKT3, ALDH3A1, ALOX5, ALPL, ANG, ANGPT1, ANGPT2, ANGPT4, APP, APPBP2, AR, ARHA, ARHC, ARHI, ARHU, ARNT, ASC, ATP7B, ATRX, AZGP1, BAK1, BAX, BCAR1, BCAS1, BCAS2, BCL10, BCL2, BCL2L1, BCL6, BGLAP, BIN1, BIRC5, BRCA1, BRIP1, BZRP, C11ORF17, CA12, CA9, CAB2, CALCR, CANX, CASP3, CASP6, CASP8, CASP9, CASR, CAT, CAV1, CBFA2T3, CCL2, CCL4, CCL5, CCNC, CCND1, CCND2, CCND3, CCR7, CD14, CD24, CD34, CD4, CD44, CD59, CD9, CDC2, CDC25A, CDC25B, CDC42, CDH1, CDH13, CDK10, CDK2, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2B, CDKN2C, CDKN2D, CEACAM1, CEACAM5, CEACAM6, CEBPA, CGA, CHI3L1, CHK, CHUK, CLDN1, CLU, CNR1, COL18A1, COMT, CSE1L, CSF3, CSH1, CSH2, CSPG2, CST6, CTGF, CTSB, CTSD, CUTL1, CXCL10, CXCL12, CXCR4, CYP1A1, CYP1B1, CYP2D6, CYR61, DAB2, DAPK1, DCN, DDR1, DFFB, DPH2L1, DSC3, DSP, DTYMK, DUSP1, EDNRA, EEF1A2, EEF2, EFNA1, EGFR, EGR1, EIF2S1, EIF4E, ELF3, EMP1, EMS1, ENG, ENO1, ENO2, EPAS1, EPHA2, EPO, EPOR, ERBB2, ERBB4, ESRRA, ETS2, ETV4, EXTL3, F2, F2R, F2RL1, F3, FABP3, FADS2, FANCA, FASN, FBLN5, FBXW7, FES, FGF1, FGF5, FGF8, FGFR1, FGFR2, FHL2, FIGF, FKBP4, FLT1,

		FLT4, FN1, FOS, FOSB, FOSL1, FOSL2, FRAT1, FRZB, FTH1, FURIN, FXYD3, G22P1, G6PD, GALNT3, GAPD, GARP, GHR, GPC1, GPR30, GRB2, GRB7, GRPR, GSN, GSTA2, GSTM1, GSTM3, GSTP1, GZMB, HDAC1, HES1, HMGA1, HMGB1, HMGCR, HOXA1, HOXB7, HP, HSD17B1, HSF1, HSPA5, HSPCA, HSPG2, ID1, IFNG, IGF1R, IGF2, IGF2R, IGFBP1, IGFBP2, IGFBP4, IGFBP5, IGSF4, IL10, IL13, IL15, IL18, IL1A, IL1B, IL1RN, IL2RA, IL3, IL6R, IL6ST, ILK, IMP-1, ING1, IRS2, ISGF3G, ITGA2, ITGA3, ITGA6, ITGB5, JAK2, JUN, JUNB, JUP, KAI1, KCNH1, KIT, KITLG, KLF4, KLF5, KLK10, KLK13, KLK3, KRT14, KRT18, KRT7, KRTHB1, LAMP3, LAMR1, LASP1, LCP1, LEP, LGALS1, LMNA, LOX, LRP1, LTA, LTF, LY75, LZTS1, MAD2L1, MADH3, MADH4, MAP2K4, MAP3K8, MAP4, MAPK1, MAPK14, MAPK3, MAPK8, MAPKAPK2, MATK, MAX, MBD2, MCC, MDM2, ME1, MEN1, MEST, MFGE8, MLN51, MMP1, MMP13, MMP2, MMP9, MNT, MRE11A, MSF, MSLN, MST1R, MT1B, MT1X, MT2A, MTA1, MTHFR, MUC1, MYCL1, MYOD1, NBL1, NBS1, NCAM1, NCOA2, NCOA4, NCOR1, NCOR2, NEK4, NF1, NGFR, NME1, NOS3, NOV, NPY, NQO1, NR1I2, NR2C1, NR2F2, NR2F6, NR3C1, NR4A1, NRG1, NRIP1, ORM1, ORM2, OSMR, P8, PACE4, PAK1, PBOV1, PCAF, PCSK1, PDGFB, PECAM1, PEPD, PFN1, PGC, PGGT1B, PHB, PIK3R1, PIP, PKD1, PKM2, PLAB, PLAT, PLAU, PLCG1, PLD2, PLU-1, POMC, POR, PPM1D, PPP1CC, PPP2R1B, PRDM2, PRKAR1A, PRKCG, PRKCM, PRKCZ, PRKR, PRLR, PRSS8, PTAFR, PTCRA, PTGS1, PTK2B, PTK6, PTMA, PTN, PTPN1, PTPN6,PTPRF, PTPRG, PTPRJ, PXN, PYGM, RAD51, RAD52, RAD54L, RARG, RASSF1, RB1, RBBP1, RBL2, RBP1, RBP1L1, REA, RELA, RPA1, RPL19, RPS6KB1, RRAD, S100A7, SCD, SCGB1D2, SCGB3A1, SDC1, SEL1L, SELE, SELP, SERPINB5, SERPINE1, SERPINF1, SERPINI2, SFN, SFRP1, SHC1, SIAH1, SIAT6, SKP2, SLC19A1, SLC22A1L, SLC2A1, SLC2A3, SLC2A4, SLC2A5, SLC5A5, SNAI1, SNCB, SNCG, SOX4, SP1, SPARC, SPDEF, SPG7, SPINT1, SQSTM1, SRC, SRD5A2, SRF, SSTR1, SSX2, ST14, ST7, STARD3, STAT1, STAT2, STAT6, STC1, STE, STS, SULT1A1, SYK, TAC1, TACC1, TAGLN, TBX2, TDGF1, TEK, TERF1, TERT, TFAP2C, TFRC, TGFB3, TGFBR2, TGFBR3, TGM2, THBD, THPO, TIAM1, TIE, TIEG, TIMP2, TIMP4, TJP1, TJP2, TK1, TMSB10, TNC, TNF, TNFRSF1B, TNFRSF5, TNFSF10, TNFSF6, TP53, TP73, TPD52, TPM2, TRAF4, TSP50, TTC4, TXN, UGT1A1, USF1, USF2, VCL, VDR, VLDLR, VWF, WHSC1L1, WISP1, WISP2, WNT1, WNT10B, WNT2, WT1, WWOX, XLKD1, XRCC2, XRCC3 AND XRCC5.
62	Small cell	ABCC3, ACTB, ADCYAP1, ANXA2, AVP, AXL, BAX, BCL2, BCL2L1, CALCA, CASP8, CCKBR, CCL2, CCND1, CD24, CD74, CD9, CDC2, CDH13, CDH6, CDK6, CDKN1A, CDKN1B, CDKN2B, CDKN2D, CHGA, CHGB, CSF3, DES, DNMT3B, DRD2, EGFR, ENO2, EPHA3, EPHB2, EPO, ERBB2, FOSL1, GSTM1, GSTP1, HNRPA2B1, HYAL2, IFNG, IL15, IL1B, IL1RN, IL2RA, ITGA9, KIT, KITLG, LCK, MAPK3, MEN1, MHC2TA, MME, MMP2, MPO, MST1, MXI1, MYCN, NCAM1, NF1, NOTCH1, NPPA, NR3C1, OXT, PCSK1, PLCB1, PLCL1, POMC, PPP1R3A, PRKCM, PTK2B, PTN, PXN, RASSF1, RB1, RBM6, RCV1, SEMA3B, TAC1, TCTA, TF, TGFBR2, THBD, TITF1, TNF, TOP2B, TP53, USP4, VIP AND VIPR1.
83	Nonsmall Cell lung carcinoma	ABCC3, ACE, AGER, AKT1, AMFR, ANGPT1, BAI1, BAK1, BAX, BCL2, BCL2L1, BIRC4, BIRC5, BUB1, CA9, CACNA2D2, CASP3, CASP5, CASP8, CASP9, CAT, CCL2, CCL4, CCL5, CCND1, CD151, CD24, CD44, CD74, CD9, CDC2, CDC25A, CDC25B, CDH13, CDK2, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2B, CDKN2C, CEACAM5, CEACAM6, CHGA, COL18A1, CSF3, CTAG2, CTNND1, CTSB, CXCL10, CXCL5, CYR61, DAPK1, DIA1, DKK3, DNMT3B, EGFR, EGR1, ENG, ENO2, EPAS1, EPB41L3, EPHA2, EPHA3, EPO, ERBB2, ETV4, F2, F3, FADD, FGFR1, FLT1, FLT4, FOS, FUT7, GSN, GSTM1, GSTP1, HNRPA2B1, HOXA10, HSPG2, HYAL2, IFNG, IGFBP6, IGSF4, IL10, IL10RA, IL1A, IL24, IL2RA, IL3, IL6ST, IRF1, ITGA11, ITGA5,

		ITGA9, JUN, JUP, KAI1, KITLG, KRT18, LAMC2, LAMR1, LBP, LEP, LMNA, LZTS1, MADH4, MAPK3, MDM2, MECP2, MME, MMP2, MMP9, MST1R, MTAP, MUC1, MUC4, MYCL1, NCAM1, NME1, NQO1, OGG1, PECAM1, PKM2, PLAT, PLAU, PLCL1, PLK, POLK, PPP1R3A, PTGS1, PTN, RASSF1, RB1, RBL2, RNF7, RPA1, RPS6KA1, RXRG, SELE, SEMA3B, SLC2A1, SLC2A3, SLPI, SSA1, TBXA2R, TDGF1, TEK, TERT, TFRC, TGFBR2, TGM1, TGM2, TNF, TNFRSF5, TNFSF10, TNFSF6, TP53, TXN, VIP, VIPR1 AND WT1.
146	Colore Ctal cancer	ABCD3, ABL1, ACTB, ADPRT, AKT3, ALOX15, ANG, ANGPT2, ANPEP, APBA1, APBA2, APOBEC1, AR, ARHA, ARHU, ATF3, ATRX, AURKB, AXIN2, AXL, BAI1, BAK1, BAX, BCAS1, BCL10, BCL2, BCL2L1, BIRC4, BIRC5, BRAF, BRCA1, BUB1, CA9, CACNA1G, CALB2, CALR CASP3, CASP5, CASP8, CASP9, CAT, CAV1, CCKBR, CCND1, CCND2, CD14, CD44, CD59, CD9, CDC2, CDC25A, CDC25B, CDC42, CDH13, CDK2, CDK4, CDK6, CDKN1A, CDX1, CDX2, CEACAM1, CEACAM5, CEACAM6, CES2, CHK, CHST2, CLDN1, CSE1L, CST3, CSTB, CTAG1, CTNNA1, CTNNBIP1, CTNND1, CTSB, CTSD, CXCL10, CYP1A1, CYP1A2, CYP1B1, CYP27B1, DAF, DAPK1, DCC, DCN, DDX6, DNMT3B, DPP4, DTR, DUSP1, DUT, ECE1, EDNRA, EFNA1, EFNB2, EGFR, EIF4E, ENC1, ENG, EPHA2, ERBB2, ERBB4, EREG, ETS2, EXTL3, F2, F3, FACL4, FADD, FASN, FBLN5, FDXR, FGFR1, FGFR3, FIGF, FLJ11383, FLJ22795, FLT1, FLT4, FN1, FOSL1, FPGS, FURIN, FUT1, FUT8, FZD10, G6PD, GALNT3, GAPD, GAS, GJB1, GPA33, GRPR, GSTA1, GSTM3, GUCA2A, GUCA2B, GUCY2C, HD, HGFAC, HIP1, HLA-DRB3, HMGA1, HMGCR, HOXB6, HOXB8, HSD17B1, HSD17B2, HSPA5, IFNG, IGF2, IGF2R, IGFBP1, IGFBP2, IGFBP4, IL10, IL13, IL18, IL1A, IL2RA, IL7, IMP-1, ITGA2, ITGA3, ITGA5, ITGA6, ITGAL, ITGB3, JAK2, JUN, JUP, KAI1, KIT, KITLG, KLF4, KRAS2, LAMC2, LAMP1, LAMP2, LAMP3, LAMR1, LCK, LCN2, LDLR, LEF1, LGALS1, LMNA, LTA, MADH3, MAP2K4, MAPK1, MAPK14, MAPK3, MBD2, MBD4, MCC, MDK, MDM2, MEP1A, MEST, MGAT5, MMP1, MMP2, MMP9, MSH6, MSLN, MST1R, MTHFR, MTR, MUC4, MYCL1, MYOD1, NCAM1, NDRG1, NF1, NMB, NMT1, NOTCH1, NPR3, NQO1, NRAS, NUMA1, OGG1, OGT, OPHN1, PBOV1, PCBD, PDGFB, PGF, PIGR, PIK3R1, PKM2, PLA2G2A, PLAT, PLAU, PLCD1, PLCG1, PLD2, PLK, PPARD, PPP1R3A, PPP2R1B, PRDM2, PRF1, PRKCG, PRKDC, PRKR, PRSS1, PTAFR, PTGES, PTGS1, PTK6, PTMA, PTPRJ, PXN, RAD50, RAD54L, RASA1, RB1, RBP1L1, RECQL, RFC3, RNF7, RPA1, RPL29, RPN2, S100A6, SCD, SDC1, SELE, SEPP1, SFRP1, SIAH1, SIAT6, SKP2, SLC16A1, SLC2A1, SLC3A2, SLC7A5, SPARC, SPG7, SPINT1, SPN, SRC, SREBF2, SSX2, ST14, ST7, STAT1, TCF7, TDGF1, TERT, TFAP2A, TFF3, TFRC, TGFB3, TGFBR2, THBD, TIA1, TIMP2, TJP2, TK1, TMEFF2, TMSB10, TNC, TNF, TNFRSF10C, TNFRSF1B, TNFSF10, TNFSF6, TP53, TP73, TP73L, TPT1, TRA1, VCL, VDR, VIP, VTN, WISP1, WISP2, WNT2, XRCC5, YES1 AND ZNF151.

Delete paragraph 0600 and replace it with the following paragraphs:

Table 14 lines 31-44, 88-103, 123-134, 192-210, 238-242, 342-351, 426-439, 451-453, 547-549, 608, 671-688 comprises sequence data of GAMs associated with different diseases. Each row referrs to a specific disease, and lists the SEQ ID NOs of GAMs that target genes associated with that disease. The table contains the following fields: ROW#: index of the row number; DISEASE NAME: name of the disease; SEQ ID NOs OF GAMS ASSOCIATED WITH DISEASE: list of sequence listing IDs of GAMs targeting genes that are associated with the specified disease;

ROW	DISEASE NAME	SEQ ID NOs OF GAMS ASSOCIATED WITH DISEASE
4	Prostate cancer	2, 3, 4, 5, 10, 13, 14, 16, 18, 19, 21, 22, 23, 24, 26, 27, 30, 32, 33, 34, 35, 38, 39, 41, 42, 44, 45, 46, 50, 52, 53, 54, 56, 57, 59, 60, 62, 64, 65, 66, 67, 68, 69, 71, 73, 74, 77, 78, 80, 82, 84, 88, 93, 94, 97, 99, 102, 103, 104, 105, 106, 108, 109, 111, 112, 114, 115, 116, 118, 119, 120, 121, 123, 125, 126, 128, 130, 133, 135, 136, 137, 139, 142, 143, 144, 146, 147, 148, 149, 150, 151, 152, 154, 155, 156, 159, 161, 165, 166, 168, 170, 171, 172, 173, 175, 177, 179, 180, 181, 183, 184, 185, 192, 194, 195, 196, 199, 201, 202, 203, 204, 207, 210, 212, 213, 214, 217, 218, 219, 220, 221, 228, 229, 230, 232, 234, 235, 237, 238, 240, 241, 243, 244, 246, 248, 249, 251, 252, 253, 255, 257, 258, 259, 260, 261, 262, 264, 266, 268, 269, 270, 271, 272, 273, 274, 278, 281, 283, 284, 285, 287, 288, 290, 293, 295, 296, 297, 299, 300, 301, 305, 306, 309, 311, 312, 314, 315, 316, 318, 319, 324, 326, 329, 334, 335, 337, 338, 339, 340, 343, 344, 345, 346, 348, 349, 351, 352, 353, 354, 355, 359, 360, 361, 362, 363, 365, 369, 370, 371, 372, 375, 376, 377, 379, 380 and 9650118-9780695.
16	Lung cancer	1, 2, 3, 4, 5, 7, 9, 10, 11, 12, 13, 14, 15, 18, 21, 22, 23, 24, 25, 26, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 41, 44, 45, 46, 49, 50, 51, 54, 55, 57, 58, 59, 60, 61, 62, 63, 65, 66, 67, 68, 69, 70, 71, 73, 74, 75, 76, 77, 78, 80, 81, 82, 84, 85, 86, 87, 88, 92, 93, 94, 97, 98, 99, 102, 104, 105, 106, 108, 112, 113, 115, 118, 119, 120, 121, 122, 123, 125, 126, 127, 128, 130, 131, 132, 133, 135, 136, 137, 138, 139, 144, 146, 147, 148, 149, 150, 151, 152, 154, 155, 157, 158, 159, 160, 162, 163, 164, 166, 168, 170, 171, 172, 173, 174, 176, 177, 178, 179, 180, 181, 182, 183, 184, 189, 193, 194, 195, 196, 197, 199, 201, 202, 203, 204, 205, 206, 209, 210, 212, 213, 214, 215, 217, 218, 221, 222, 224, 225, 228, 229, 230, 231, 232, 234, 235, 236, 237, 239, 240, 241, 242, 243, 244, 245, 246, 248, 251, 252, 255, 259, 260, 261, 262, 264, 265, 268, 269, 270, 271, 274, 275, 279, 283, 284, 285, 287, 288, 290, 291, 292, 293, 296, 297, 298, 299, 301, 304, 305, 306, 307, 308, 309, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 326, 329, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 343, 344, 345, 346, 348, 349, 350, 351, 352, 353, 354, 355, 357, 359, 360, 361, 362, 363, 364, 365, 367, 368, 369, 370, 371, 373, 375, 376, 380 and 8843701-9042597.
24	HIV	2, 5, 7, 9, 10, 13, 18, 21, 22, 23, 24, 25, 26, 30, 31, 32, 33, 35, 38, 39, 42, 43, 44, 45, 47, 50, 51, 52, 53, 54, 55, 57, 61, 62, 64, 65, 67, 68, 69, 71, 73, 74, 80, 81, 82, 84, 85, 92, 93, 94, 97, 99, 102, 106, 107, 108, 109, 112, 115, 116, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 130, 131, 133, 137, 138, 139, 144, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 159, 160, 165, 166, 168, 173, 174, 175, 177, 178, 179, 182, 185, 193, 194, 195, 196, 197, 198, 201, 202, 203, 210, 212, 213, 214, 215, 218, 222, 228, 229, 230, 231, 232, 233, 234, 237, 238, 239, 240, 241, 242, 246, 248, 249, 251, 252, 259, 260, 262,264 , 268, 269, 271, 272, 278, 279, 283, 284, 290, 291, 293, 296, 298, 299, 301, 305, 306, 308, 309, 311, 316, 317, 318, 323, 326, 329, 334, 335, 336, 337, 338, 339, 340, 341, 344, 345, 346, 352, 353, 354, 356, 359, 360, 361, 362, 363, 365, 367, 370, 371, 372, 375, 377, 380 and 8475487-8574405.

37	Breast cancer	2, 3, 4, 5, 7, 9, 10, 12, 13, 14, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 41, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 71, 73, 74, 76, 77, 78, 79, 80, 81, 82, 84, 86, 87, 88, 92, 93, 94, 96, 97, 98, 99, 100, 102, 103, 104, 105, 106, 107, 108, 109, 111, 112, 115, 116, 118, 119, 120, 121, 122, 123, 125, 126, 127, 128, 130, 131, 132, 133, 135, 136, 137, 138, 139, 143, 144, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 165, 166, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 190, 191, 192, 193, 194, 195, 196, 197, 199, 201, 202, 203, 204, 205, 206, 207, 209, 210, 211, 212, 213, 214, 215, 217, 218, 219, 220, 221, 222, 225, 228, 229, 230, 231, 232, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 248, 249, 251, 252, 254, 255, 256, 257, 259, 260, 261, 262, 263, 264, 265, 266, 268, 269, 270, 271, 272, 274, 277, 278, 279, 280, 281, 283, 284, 285, 286, 287, 288, 290, 291, 292, 293, 294, 296, 297, 298, 299, 301, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 321, 322, 323, 324, 326, 327, 328, 329, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 343, 344, 345, 346, 348, 349, 350, 351, 352, 353, 354, 355, 357, 359, 360, 361, 362, 363, 364, 365, 367, 368, 369, 370, 371, 373, 375, 376, 377, 380 and 7388386-7729593.
42	Encephalitis	2, 10, 12, 22, 26, 33, 34, 35, 44, 45, 50, 54, 55, 57, 65, 67, 69, 81, 82, 97, 99, 105, 106, 108, 112, 118, 119, 120, 121, 122, 124, 125, 126, 146, 150, 159, 168, 173, 195, 197, 212, 213, 214, 229, 234, 246, 251, 259, 262, 265, 268, 271, 283, 284, 287, 290, 309, 311, 316, 333, 334, 335, 337, 339, 345, 346, 348, 352, 353, 357, 361, 370 and 8298833-8314921.
62	Small cell carcinoma	2, 5, 10, 11, 13, 14, 18, 21, 22, 24, 26, 29, 33, 35, 38, 39, 41, 45, 49, 50, 51, 54, 57, 58, 59, 63, 65, 66, 67, 68, 69, 73, 78, 80, 81, 82, 93, 94, 97, 99,106, 108, 112, 118, 119, 120, 121, 122, 125, 126, 130, 131, 133, 135, 136, 137, 139, 146, 147, 148, 149, 151, 152, 154, 155, 157, 159, 160, 164, 166, 172, 173, 174, 179, 180, 183, 184, 185, 189, 193, 194, 195, 202, 203, 209, 210, 212, 213, 214, 218, 222, 224, 228, 229, 230, 232, 234, 235, 237, 240, 241, 242, 246, 248, 251, 252, 259, 261, 262, 264, 265, 268, 271, 274, 277, 279, 283, 287, 288, 290, 291, 296, 299, 305, 306, 308, 309, 311, 312, 318, 324, 326, 329, 332, 334, 335, 337, 338, 339, 340, 344, 345, 349, 352, 353, 354, 359, 361, 362, 363, 364, 365, 368, 369, 370, 375, 376, 380 and 9954731-10022876.
83	Nonsmall cell lung	1, 2, 3, 4, 7, 9, 10, 15, 17, 18, 21, 22, 23, 24, 25, 27, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 43, 44, 46, 49, 50, 51, 54, 55, 58, 61, 62, 63, 65, 66, 67, 68, 69, 70, 71, 73, 74, 75, 77, 78, 80, 81, 82, 84, 87, 88, 92, 93, 94, 97, 99, 102, 104, 106, 107, 108, 109, 112, 116, 118, 119, 120, 121, 123, 125, 126, 128, 129, 130, 131, 133, 134, 135, 136, 137, 138, 144, 146, 147, 148, 149, 150, 151, 152, 154, 155, 157, 158, 159, 163, 166, 168, 170, 171, 172, 173, 174, 177, 178, 179, 180, 182, 183, 185, 193, 194, 195, 196, 199, 203, 204, 205, 206, 209, 210, 212, 213, 214, 215, 216, 218, 221, 222, 228, 230, 231, 232, 234, 235, 237, 241, 242, 243, 244, 246, 248, 251, 252, 255, 259, 260, 262, 264, 268, 269, 271, 274, 279, 283, 284, 285, 286, 287, 288, 290, 291, 292, 293,

		299, 301, 304, 305, 306, 308, 309, 311, 312, 314, 317, 318, 320, 321, 322, 323, 324, 326, 329, 332, 333, 334, 335, 337, 339, 340, 343, 344, 345, 346, 348, 349, 351, 352, 353, 354, 355, 359, 360, 361, 362, 363, 364, 365, 368, 369, 370, 371, 373, 375, 376 and 9409578-9523950.
88	Pancreatic cancer	21, 33, 39, 45, 54, 62, 63, 76, 78, 80, 84, 95, 97, 99, 106, 137, 139, 145, 147, 159, 168, 248, 256, 262, 264, 266, 269, 271, 279, 283, 285, 294, 297, 334, 335, 339, 343, 362 and 9568057-9575513.
113	Psoriasis	4, 5, 21, 23, 35, 45, 46, 50, 52, 54, 68, 69, 92, 93, 99, 106, 109, 125, 126, 130, 134, 147, 148, 149, 159, 168, 196, 203, 205, 214, 222, 228, 248, 268, 271, 283, 299, 309, 326, 334, 335, 337, 360, 363, 365, 368, 371 and 9780696-9788989.
130	E.coli	10, 45, 46, 159, 168, 230, 248, 268, 306 and 8291234-8294531.
146	Colorectal cancer	1, 2, 3, 4, 5, 7, 9, 10, 12, 13, 14, 15, 17, 18, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 46, 47, 48, 49, 50, 51, 52, 54, 55, 57, 58, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 73, 74, 75, 76, 77, 78, 80, 81, 82, 84, 85, 86, 87, 88, 90, 92, 93, 94, 96, 97, 98, 99, 100, 102, 103, 105, 106, 107, 108, 109, 110, 112, 113, 116, 118, 119, 120, 121, 122, 123, 125, 126, 127, 128, 130, 133, 134, 135, 136, 137, 138, 139, 142, 143, 144, 146, 147, 148, 149, 150, 151, 152, 154, 155, 156, 157, 159, 160, 162, 163, 165, 166, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 181, 182, 183, 184, 185, 186, 189, 190, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 209, 210, 211, 212, 213, 214, 215, 217, 218, 220, 221, 222, 223, 228, 229, 230, 231, 232, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 246, 248, 249, 251, 252, 255, 259, 260, 261, 262, 263, 264, 266, 268, 269, 270, 271, 274, 279, 281, 283, 284, 285, 286, 288, 290, 291, 292, 293, 296, 297, 298, 299, 301, 304, 305, 306, 307, 308, 309, 311, 312, 313, 314, 315, 316, 317, 318, 319, 321, 322, 323, 324, 326, 327, 329, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 343, 344, 345, 346, 348, 349, 350, 351, 352, 353, 354, 355, 357, 359, 360, 361, 362, 363, 364, 365, 367, 368, 369, 370, 371, 373, 375, 376, 377, 380 and 7810059-8039098.